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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/748,117

12/29/2003

Derek O'Hagan

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07/21/2010

NOVARTIS VACCINES AND DIAGNOSTICS INC.

INTELLECTUAL PROPERTY- X100B

P.O. BOX 8097

Emeryville, CA 94662-8097

EXAMINER

MINNIFIELD, NITA M

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/748,117	<b>Applicant(s)</b> O'HAGAN, DEREK	
	<b>Examiner</b> N. M. Minnifield	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28,32,35-74,78 and 81-91 is/are pending in the application.
- 4a) Of the above claim(s) 2,17,32,35-74,78 and 81-85 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 3-16 18-28 86-90 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

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## DETAILED ACTION

1. Applicants' amendment filed May 12, 2010 is acknowledged and has been entered. Claims 29-31, 33, 34, 75-77, 79 and 80 have been canceled. New claims 89 and 90 have been added. Claims 1-28, 32, 35-74, 78 and 81-90 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.
2. Claims 2, 17, 32, 35-74, 78 and 81-85 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 16, 2007.
3. Claims 1, 3-16, 18-28 and 86-90 have been examined in the instant application.
4. The following is a quotation of the second paragraph of 35 U.S.C. 112:  

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
5. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the limitation "four to eight" as it relates to the linear alkane group in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1, which claim 4 depends, recites the limitation of "6 to 20" as it relates to the linear alkane group. The range recite in claim 4 is outside the range of "6 to 20" and does not further limit claim 1.
6. The following is a quotation of the first paragraph of 35 U.S.C. 112:  

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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7. Claims 1, 3-16, 18-28 and 86-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising those components in the immunogenic compositions set forth in Tables 2,3A-3C, does not reasonably provide enablement for an immunogenic composition comprising any combination of possible components as set forth in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to immunogenic compositions comprising water, a polymer microparticle, an antigen adsorbed to the microparticle and a synthetic phospholipid. The claims and specification also define various synthetic phospholipids as well as polymers. The antigen can be adsorbed or entrapped on or within the microparticles. The claims defined a broad spectrum of antigens. The specification teaches numerous adjuvants for use in the immunogenic compositions.

The specification is only enabled for those immunogenic compositions set forth in the instant specification shown in Tables 2 and 3A-3C, for example PLG/MenB +sol Eisai 53 or MF59/Eisai 57 + sol gp120. The specification does not enable the full scope of the genus of the claimed immunogenic compositions.

For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. MPEP 2164.02

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re Fisher, 427 F.2d 833,839, 166 USPQ 18,24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information

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needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004)

("Nascent technology, however, must be enabled with a specific and useful teaching." The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." (citations omitted)). MPEP 2164.03

With regard to the state of the art for the claimed invention, it is noted that there is unpredictability with regard to making and using adjuvants as asserted by Applicants and the art. Edelman (Molecular Biotechnology, 2002, 21/2:129-148) teaches that the state of the art for combining adjuvants is unpredictable. "Every adjuvant has a complex and often multi-factorial immunological mechanism, usually poorly understood in vivo. Many determinants of adjuvanticity exist, and each adjuvanted vaccine is unique. Adjuvant safety is critical and can enhance, retard, or stop development of an adjuvanted vaccine. The choice of an adjuvant often depends upon expensive experimental trial and error, upon cost and upon commercial availability." (abstract) Examples of adjuvant formulations tested in humans with a variety of antigens (and with variable success) include various combinations (see p. 130, section 2.2). Edelman also teaches that "One must remember that in vivo, most adjuvants have complex and multifactorial immunological mechanisms, often poorly understood. The immunological mechanisms utilized by many adjuvants are under investigation. Such investigations will provide answers to some of the following questions. Does the adjuvant induce cell mediated (Th1) immunity, humoral (Th2) immunity, or a balance of Th1 and Th2? Which Ig isotypes dominate? Which cytokines are induced? Are CD4+ T-helper cells or CD8+ cytotoxic T-lymphocytes induced? The list of such questions is extensive, and grows in proportion to our understanding of immunological mechanisms in general." (p. 134, section 4.1) "The ability of adjuvants to influence so many parameters of the immune response greatly complicates the process of finding an effective adjuvant. This is because our knowledge of how any one adjuvant operates on a cellular level is insufficient to support a completely rational approach for matching the vaccine

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antigen with the proper adjuvant." (p. 135, section 5) Spickler et al (J. Vet. Intern. Med., 2003, 17:273-281) teaches that "The results of combining adjuvants depends on the mechanism of action and toxicity of each individual component. Combinations may be better, similar to, or worse than the individual components." (p. 278) As pointed out by Applicants, "adjuvant science is anything but predictable. Indeed, when it comes to adjuvants, there are a near-infinite number of possible combinations that are available to the ordinarily skilled artisan, none of which is predictable." (see p.22 of Remarks filed May 20, 2009)

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated: [I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof. [Footnote omitted.]

The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. In *re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); In *re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In *re Soll*, 97

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F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. MPEP 2164.03

While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01 (a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. This can be done by making specific findings of fact, supported by the evidence, and then drawing conclusions based on these findings of fact. For example, doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation. In such a case, the examiner should specifically identify what information is missing and why one skilled in the art could not supply the information without undue experimentation. See MPEP § 2164.06(a). References should be supplied if possible to support a prima facie case of lack of enablement, but are not always required. In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). However, specific technical reasons are always required. MPEP 2164.03

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

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Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) specification with respect to the genus of the claimed immunogenic compositions, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). With regard to (4) the nature of the invention and 5) the state of the prior art, these have been discussed above. One of skill in the art would require guidance and undue experimentation, in order to make and use the numerous species of adjuvant combinations claimed and set forth in the instant specification in view of the unpredictability as shown in the state of the art. The claims are enabled for those immunogenic compositions as set forth in Tables 2 and 3A-3C as set forth in the specification.

The rejection is maintained for the reasons of record. Applicant's arguments filed May 12, 2010 have been fully considered but they are not persuasive. Applicant has asserted that:

“With regard to the description regarding how to make the claimed invention, all presently pending claims under examination concern an immunogenic composition that comprises: (a) water; (b) a polymer microparticle; (c) an antigen adsorbed to the microparticle; and (d) a synthetic phospholipid compound. Disclosed throughout the present specification, including the working examples, are methods of making the claimed immunogenic compositions. Regarding phospholipids see, for instance, paragraphs [0064] to [0081] and the references set forth therein; regarding antigens see, for instance, paragraphs [0082] to [0092] and the references set forth therein; regarding microparticles, including how to form them and how to associate species such as antigens and phospholipids with them (e.g., adsorption, entrapment, etc.) see, for instance, paragraphs [0120] to [0137] and the references set forth therein. See also Examples 1-3.

Accordingly, it is respectfully submitted that, based on the present disclosure, one skilled in the art could readily make the claimed invention without undue experimentation, indeed, with little to no experimentation.

With regard to the description as to how to use the claimed invention, the specification describes numerous ways of administering the immunogenic compositions of the claimed invention, including various modes of injection, nasal administration, mucosal administration,

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intraocular administration, rectal administration, vaginal administration, oral administration, pulmonary administration, and so forth. See, e.g., paragraphs [0145] to [00149] and the references set forth therein, as well as Example 3.

Concerning the immunogenic aspect of immunogenic composition claims 1, 3-16, 18-28 and 86-88 under examination, as defined in the present specification, by an "antigen" is meant a molecule that contains one or more epitopes capable of stimulating a host's immune system. Antigens defined thusly are readily available and well-known in the art. See, e.g., paragraphs [0082] to [0092] and the references set forth therein. Because antigens are, by definition, capable of stimulating an immune response in a host, composition claims 1, 3-16, 18-28 and 86- 88 under examination are clearly immunogenic. In other words, even assuming solely for the sake of argument that the claimed combination of adjuvants (i.e., polymer microparticle and synthetic phospholipid) were to have no impact on the immunogenicity of the composition, the composition would nonetheless stimulate an immune response because the antigen in the composition, by definition, will contain one or more epitopes capable of stimulating the host's immune system." (Remarks, pp. 18-19)

However, it is the Examiner's position that the specification does not enable the broad scope of the instantly claimed invention. It is noted that this is not a lack of enablement based on written description, the claimed invention has been described as shown by Applicant's statements above. Applicant has set forth a large genus of immunogenic compositions comprising among other components a very large genus of synthetic phospholipids (see claims 1 and 7-9 for example). For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re

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Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The “amount of guidance or direction” refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) (“Nascent technology, however, must be enabled with a specific and useful teaching.” The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee’s instruction. Thus, the public’s end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology.” (citations omitted)).<

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[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

Footnote omitted.]

The scope of the required enablement varies inversely with the degree of predictability

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involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. In re Vickers, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); In re Cook, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. MPEP 2164.03

With regard to the state of the art for the claimed invention, it is noted that there is unpredictability with regard to making and using adjuvants as asserted by Applicants and the art. Edelman (Molecular Biotechnology, 2002, 21/2:129-148) teaches that the state of the art for combining adjuvants is unpredictable. "Every adjuvant has a complex and often multi-factorial immunological mechanism, usually poorly understood in vivo. Many determinants of adjuvanicity exist, and each adjuvanted vaccine is unique. Adjuvant safety is critical and can enhance, retard, or stop development of an adjuvanted vaccine. The choice of an adjuvant often depends upon expensive experimental trial and error, upon cost and upon commercial availability." (abstract) Examples of adjuvant formulations tested in humans with a variety of antigens (and with variable success) include various combinations (see p. 130, section 2.2). Edelman also teaches that "One must remember that in vivo, most adjuvants have complex and multifactorial immunological mechanisms, often poorly understood. The immunological mechanisms utilized by many adjuvants are under investigation. Such investigations will provide answers to some of the following questions. Does the adjuvant induce cell mediated (Th1) immunity, humoral (Th2) immunity, or a balance of Th1 and Th2? Which IG isotypes dominate? Which cytokines are induced? Are CD4+ T-helper cells or CD8+ cytotoxic T-lymphocytes induced? The list of such questions is extensive, and grows in proportion to our understanding

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of immunological mechanisms in general." (p. 134, section 4.1) "The ability of adjuvants to influence so many parameters of the immune response greatly complicates the process of finding an effective adjuvant. This is because our knowledge of how any one adjuvant operates on a cellular level is insufficient to support a completely rational approach for matching the vaccine antigen with the proper adjuvant." (p. 135, section 5) Spickler et al (J. Vet. Intern. Med., 2003, 17:273-281) teaches that "The results of combining adjuvants depends on the mechanism of action and toxicity of each individual component. Combinations may be better, similar to, or worse than the individual components." (p. 278) As pointed out by Applicants, "adjuvant science is anything but predictable. Indeed, when it comes to adjuvants, there are a near-infinite number of possible combinations that are available to the ordinarily skilled artisan, none of which is predictable." (see p.22 of Remarks filed May 20, 2009)

Further, while the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. This can be done by making specific findings of fact, supported by the evidence, and then drawing conclusions based on these findings of fact. For example, doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation. In such a case, the examiner should specifically identify what information is missing and why one skilled in the art could not supply the information without undue experimentation. See MPEP § 2164.06(a). References should be supplied if possible to support a prima facie case of lack of enablement, but are not always required. In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). However, specific technical reasons are always required MPEP § 2164.04 This analysis has already been set forth above.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 89 and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hagan et al (WO 98/33487) taken with Hawkins et al (6290973).

O'Hagan et al teaches poly(lactide) or poly(lactide-co-glycolide) microparticles with adsorbed antigens (abstract). O'Hagan et al teaches "Particulate carriers with adsorbed or entrapped antigens have been used in an attempt to elicit adequate immune responses. Such carriers present multiple copies of a selected antigen to the immune system and promote trapping and retention of antigens in local lymph nodes. The particles can be phagocytosed by macrophages and can enhance antigen presentation through cytokine release. Examples of particulate carriers include those derived from polymethyl methacrylate polymers, as well as microparticles derived from poly(lactides) and poly(lactide-co-glycolides), known as PLG." (pp. 2-3; see also p. 7) O'Hagan et al teaches the use of microparticles with adsorbed antigens provides a safe and effective approach for enhancing the immunogenicity of a wide variety of antigens (p. 5). O'Hagan et al teaches that the microparticle has a diameter of about 100 nm to about 150  $\mu$ m, more preferably about 200 nm to about 30  $\mu$ m and most preferably about 500 nm to about 10  $\mu$ m (p. 6). O'Hagan et al teaches the claimed immunogenic composition except for a synthetic phospholipid.

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However, Hawkins et al teaches novel compounds that function as immunological adjuvants when co-administered with antigens (abstract; column 2, lines 10-13). Hawkins et al teaches the use of various synthetic phospholipids that can be used in vaccine compositions, pharmaceutical compositions or immunostimulatory compositions (cols. 3-7; cols. 187-188: ER804053, ER804057). It is noted that Hawkins et al teaches the use of the specific synthetic phospholipids set forth in the instant claims. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of O'Hagan et al with Hawkins et al to make an immunogenic composition comprising water, polymer microparticle, antigen adsorbed to microparticle and synthetic phospholipids (various phospholipids) for the purpose of immunizing a subject to increase or enhance immunogenic activity, immune response or stimulate/enhance protection against an infectious antigen for example. The claimed invention is prima facie obvious in view of the combined teachings of the prior art, absent any convincing evidence to the contrary.

The claimed invention is directed to a composition, which the combined references of O'Hagan taken with Hawkins teach. Both references teach components of the claimed invention for the same purpose, an adjuvant (see above). Therefore, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious).

In an additional embodiment, the invention is directed to a method of immunization which comprises administering to a vertebrate subject a therapeutically effective amount of the microparticle composition above. In yet an additional embodiment, the invention is directed to a

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method for eliciting a cellular immune response in a vertebrate subject comprising administering to a vertebrate subject a therapeutically effective amount of a selected viral antigen adsorbed to a poly( $\alpha$ -hydroxy acid) microparticle.” (pp. 4-6) And Hawkins teaches novel compounds (i.e. phospholipids) that function as immunological adjuvants. Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious).

The Supreme Court further stated that: When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. Id. at \_\_\_, 82 USPQ2d at 1396. When considering obviousness of a combination of known elements, the operative question is thus “whether the improvement is more than the predictable use of prior art elements according to their established functions.” Id. at \_\_\_, 82 USPQ2d at 1396.

In the instant case both O’Hagan and Hawkins teach the need for new adjuvants to help in improved immunogenicity of antigens and an improved immune response in a subject. They both teach a finite number of identified, predictable solutions, all with a reasonable expectation of success. O’Hagan et al teaches that the use of microparticles with adsorbed antigens provides

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a safe and effective approach for enhancing the immunogenicity of a wide variety of antigens (p. 5). Hawkins et al teaches novel compounds that function as immunological adjuvants when co-administered with antigens (abstract; column 2, lines 10-13). Hawkins et al teaches the use of various synthetic phospholipids that can be used in vaccine compositions, pharmaceutical compositions or immunostimulatory compositions (cols. 3-7; cols. 187-188: ER804053, ER804057).

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It is well known in the art (O'Hagan et al) to use microparticles as adjuvants in composition with antigens to create an immunogenic composition, while Hawkins et al teaches novel compounds that function as immunological adjuvants when co-administered with antigens (abstract; column 2, lines 10-13). Hawkins et al teaches the use of various synthetic phospholipids that can be used in vaccine compositions, pharmaceutical compositions or immunostimulatory compositions (cols. 3-7; cols. 187-188: ER804053, ER804057). Hawkins et al teaches the specific synthetic phospholipids (ER804053, ER804057) claimed by Applicants. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results. The claimed invention is prima facie obvious in view of the teachings of O'Hagan and Hawkins absent any convincing evidence to the contrary.

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. M. Minnifield/  
Primary Examiner, Art Unit 1645